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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,191	10/15/2001	Avi J. Ashkenazi	GNE.2630P1C4	4728

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,191	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 58-70 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 58-70 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/20/02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 58-70 are pending in the instant application. Claims 1-57 have been canceled and claims 58-70 have been added as requested by Applicant in the Preliminary Amendment filed October 15, 2001.

Specification

2.1 The disclosure is objected to because the correct priority data has not been submitted. The specification of related application 09/999,829 has been amended to recite the correct priority information, but the present application has not.

2.2 The disclosure is also objected to for containing numerous errors. For example, on page 101, lines 16 and 17 and 31-32, the PRO213-1 of SEQ ID NO: 506 is stated as having 295 amino acids, but in the sequence listing, SEQ ID NO: 506 has 273 amino acids. Also on page 309, lines 10-12, the start and stop codons recited for SEQ ID NO: 505 are incorrect.

2.3 The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See page 124, line 37, page 127, line 18, page 233, line 1, page 275, line 1, page 276, line 1, page 309, line 32, page 311, line 33, page 313, lines 5, 6, 20 and 23, at least. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Double Patenting

3. Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application. 37 CFR 1.78(b) provides that when two or more

applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application.

A sequence search of the pending and published application databases has revealed that there are a series of applications in which SEQ ID NO: 506 is present but that do not claim the polypeptide. However, due to the large number of applications that contain this sequence, the examiner is unable to determine if any of these applications have claims directed to this polypeptide. Applicant is required to point out to the Examiner all double patenting issues. See MPEP § 1.105.

The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained will be accepted as a complete reply to the requirement for that item.
This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

Determination of Priority

4. Claims 58-70 are directed to the protein of SEQ ID NO: 506, identified as PRO213-1. The instant specification discloses that PRO213-1 (SEQ ID NO: 506) is a 273 amino acid protein (Figure 213), and that the nucleic acid molecule encoding the protein (SEQ ID NO: 505) is amplified in a number of primary tumors (Table 9). Because of this, the nucleic acid of SEQ ID NO: 505 would have utility as a cancer marker, however, examination of the priority documents

is confusing and presents conflicting results concerning the PRO213-1 protein and nucleic acid and the PRO213 protein and nucleic acid (SEQ ID NOS: 1 and 2). In parent application 09/918,585, Table 9 shows the results of ΔCt values in lung and colon primary tumor and cell line models for PRO213-1, of which SEQ ID NO: 506 is the identical sequence to SEQ ID NO: 506 of the instant application, and which shows the identical results. However, provisional application 60/100,038 shows alignments between PRO213 (DNA30943-1163, SEQ ID NO: 1), PRO1330 (DNA64907-1163-1, SEQ ID NO: 2) and PRO1449 (DNA64908-1163-1, SEQ ID NO: 3) in Figure 4, and shows that these proteins are highly related. Provisional 60/131,445 also discloses PRO213, PRO1330 and PRO1449. **The sequence of the PRO1330 protein in provisionals 60/100,038 and 60/60/131,445 is identical to PRO213-1, SEQ ID NO: 506 of the instant application and is also identical to PRO1330 of SEQ ID NO: 508 of the instant application. Therefore, the exact same sequence has been given two different names (PRO213-1 and PRO1330) and is duplicated in the sequence listing, and therefore the application is not in sequence compliance.** PRO1449 of provisionals 60/100,038 and 60/131,445 is the same sequence as that of PRO1449 (SEQ ID NO: 510) of the instant application. Table 3 on page 91 of provisional 60/131,445 shows the ΔCt values in lung and colon primary tumor and cell line models for PRO213, PRO1330 and PRO1449 (second column). What is noted is that the values given for PRO213 in table 3 are identical to the values given for PRO213-1 in application 09/918,585 and the instant application, therefore, it appears that the ΔCt values of Table 9 of the instant application for PRO213-1 are actually the ΔCt values of PRO213 (SEQ ID NO: 1) of the instant application. It is also noted that the last column of Table 9 of the instant application shows the ΔCt values for PRO1330 and PRO1449,

which are identical to those of the ΔCt values of PRO213 in provisional 60/131,445, and are different from those reported for PRO1330 and PRO1440 in Table 3 of that provisional. The ΔCt values for PRO1330 (PRO213-1) disclosed in 60/131,445 demonstrate that the nucleic acid is overexpressed in several lung tumors and could be used diagnostically as such, however, that data is not present in the instant application. The effective priority date is therefore the filing date of the instant application, since the current application is not enabling for the nucleic acid of SEQ ID NO: 505.

Applicants are required to correct the instant application, and to adequately explain the discrepancies between the provisional applications and the instant applications. Applicants are warned about the possibility of introducing new matter.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 58-70 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Claims 58-70 are directed to the protein of SEQ ID NO: 506, identified as PRO213-1. The instant specification discloses that PRO213-1 is a 273 amino acid protein (Figure 213), and that the nucleic acid molecule encoding the protein (SEQ ID NO: 505) is amplified in a number of primary tumors (Table 9). Because of this, the nucleic acid of SEQ ID NO: 505 would have utility as a cancer marker (with the exception that the use of the nucleic acid is not enabled, as

explained above in the priority determination). However the protein does not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The claims are directed to isolated polypeptides having at least 80% sequence identity to the polypeptide of SEQ ID NO: 506, with or without its signal peptide, or to the extracellular domain of SEQ ID NO: 506 with or without its signal peptide. Dependent claims are directed to chimeric proteins comprising the aforementioned polypeptides. The specification contains numerous asserted utilities for the polypeptide and encoding nucleic acid at pages 190-199, including use as hybridization probes, in chromosome and gene mapping, in the generation of anti-sense RNA and DNA, to identify molecules that bind to PRO (including agonists and antagonists), to make "knock-out" mice or other animals, in gene therapy, as molecular weight markers, therapeutic agents, and for the production of antibodies. The utilities that pertain solely to nucleic acids (e.g. hybridization, chromosome and gene mapping, anti-sense) would not convey to the encoded protein. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO213-1 protein, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO213-1.

On page 309, the specification states that the PRO213-1 protein possesses unspecified homology to the human growth arrest-specific gene 6 protein, and that PRO1330 and PRO1449 polypeptide possess homology with notch4. (It is noted that PRO213-1 and PRO1330 are identical proteins, and PRO1449 differs from PRO213-1 and PRO1330 at a single amino acid at

residue 153). The specification at page 101 teaches that the proteins are believed to be useful targets for the diagnosis and/or treatment of certain cancers, and may act as predictors of the prognosis of tumor treatment, based upon the amplification of the genes encoding the proteins.

The specification at pages 331-346 describes experiments in which PRO213-1 encoding genes are asserted to be amplified in the genome of certain human lung and colon primary tumors. As discussed above, there is a problem with determining an effective priority date of the instant application, and determining what the actual ΔCt values are for this nucleic acid. Even *if* the data demonstrated a increase in copy number of PRO213-1 nucleic acids in primary tumors, such would not be indicative of a use of the encoded polypeptide as a diagnostic agent. The preliminary data were not supported by analysis of mRNA or protein expression, for example. Also, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that the protein would be useful diagnostically or as a target for cancer drug development. For example, Pennica et al. (1998, PNAS USA 95:14717-14722) teach that

> "An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See page 14722, second paragraph of left-hand column; pp.14720-14721; Pages 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors".

Gygi et al. (Molecular and Cellular Biology, March 1999, p. 1720-1730), studied over 150 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript levels; for some genes, equivalent mRNA levels

translated into protein abundances which varied by more than 50-fold. Gygi et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (abstract and Figure 5).

Thus, the data do not support the implicit assertion that polypeptide of PRO213-1 polypeptide can be used as a cancer diagnostic. Significant further research would have been required of the skilled artisan to determine whether PRO213-1 is overexpressed in any cancer to the extent that antibodies to the protein could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 58-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 58-70 are indefinite because claims 58-63, 66, 67 encompass the extracellular domain of the polypeptide of SEQ ID NO: 370. The instant application identifies the polypeptide of SEQ ID N: 370 as a chemokine, which is a secreted soluble protein, and therefore there is no "extracellular domain", since the entire protein is extracellular. The other claims are rejected for being dependent on the independent claims 58 and 63.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7.1 Claims 58-70 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the PRO213-1 polypeptide, enablement would not be found commensurate in scope with the claims. Even if there were a patentable use for the protein of SEQ ID NO: 506, variants of 80-99% identity would not be enabled because the specification has not taught one of ordinary skill in the art how to use them or fragments thereof.

7.2 Claims 58-62, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered

include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 506, with or without the signal sequence, but not the full breadth of the claims meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

7.3 Claims 58-63 and 68-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants referral to the deposit of the cDNA deposited under ATCC accession number 209791 on page 274 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. On line 34, the specification states: "This assures maintenance of a viable culture of the deposit for 30 years from the of deposit." However, this statement is incomplete. In section 2408 of the MPEP, it is stated:

"The term of deposit must satisfy the requirements of the Budapest Treaty which sets a term of at least 30 years from the date of deposit **and at least 5 years after the most recent request for the furnishing of a sample of the deposit** received by the depository."

If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an

International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 58-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 58-70 are indefinite because claims 58-63, 66, 67 encompass the extracellular domain of the polypeptide of SEQ ID NO: 506. The instant application does not identify the polypeptide of SEQ ID NO: 506 as a transmembrane protein, such as a receptor, and does not identify any extracellular or transmembrane domains, and may be a secreted protein. Therefore the term "extracellular domain" is indefinite. The other claims are rejected for being dependent on the independent claims 58 and 63.

Priority Determination

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or

abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

9. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above, the prior applications do not meet those requirements and, therefore, are unavailable under 35 U.S.C. § 120 or § 119(e). The effective priority date of the instant application is considered to be the filing date of this application, October 15, 2001, because the claimed invention is not supported by either a specific and substantial utility or a well established utility.

Rejections over Prior Art

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10.1 Claims 58-69 are rejected under 35 U.S.C. 102(e) as being anticipated by Holtzman et al., U.S. Published Patent Application 20020028508, effective priority date April 23, 1998 (09/065,363).

Claims 58-69 are drawn to polypeptides having at least 80% sequence identity, respectively, with the extracellular domain (with or without the signal sequence) or full-length protein of SEQ ID NO: 506 or polypeptide encoded by the cDNA deposited under ATCC accession number 2009791, and chimeric polypeptide further comprising a heterologous polypeptide.

Holtzman et al. disclose a protein (SEQ ID NO: 10) that is 100% identical to the protein of SEQ ID NO: 506 of the instant invention. Holtzman et al. also teaches chimeric polypeptides comprising a heterologous polypeptide (sections 0221-0224). Therefore, Holtzman et al. anticipates the claims.

10.2 Claims 58-62, 69 and 70 are rejected under 35 U.S.C. 102(e) as being anticipated by Sheppard et al., U.S. Published Patent Application 20030166907, effective priority date June 18, 1997 (09/050,143).

Claims 58-62, 69 and 70 are drawn to polypeptides having at least 80%-99% sequence identity, respectively, with the extracellular domain (with or without the signal sequence) or full-length protein of SEQ ID NO: 506 or polypeptide encoded by the cDNA deposited under ATCC accession number 2009791, and chimeric polypeptide further comprising a heterologous polypeptide which may be an epitope tag or Fc region of an immunoglobulin.

Sheppard et al. disclose a protein (SEQ ID NO: 2) that is 99% identical to the protein of SEQ ID NO: 506 of the instant invention (one conservative mismatch). Sheppard et al. also teaches chimeric polypeptides comprising a heterologous polypeptide which may be an epitope tag or Fc region of an immunoglobulin (section 0027). Therefore, Sheppard et al. anticipates the claims.

If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicate that the copy was not readily available, it is because the copy could not be readily obtained when the Office action was mailed. Should applicant desire a copy of such a provisional application, applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under 37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 70 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holtzman et al., U.S. Published Patent Application 20020028508, effective priority date April 23, 1998 (09/065,363), in view of Hopp et al., U.S. Patent Number 5,011,912, April 1991.

Claim 70 encompasses chimeric protein comprising the polypeptide of claim 58 fused to a heterologous polypeptide which may be an epitope tag or an Fc region of an immunoglobulin.

The teachings of Holtzman et al. are discussed above. Holtzman et al. does not teach expression of the protein of SEQ ID NO: 10 as a fusion protein comprising an epitope tag or Fc region.

Hopp et al. teach the use of an amino acid sequence, "ADYKDDDDK", which is disclosed as being immunogenic, for use in producing fusion protiens which can then be easily

purified. See, for example, column 2, lines 45-57. It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the protein of Holtzman et al. by producing such as a fusion protein comprising the flag amino acid sequence of Hopp et al., for the purpose of being able to easily purify the proteins of the primary references. The motivation and expectation of success are both taught by Hopp et al. who teach the flag peptide/monoclonal antibody purification system as being generally useful for such.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (571) 272-0871.

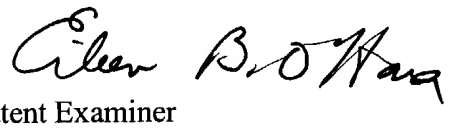
The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, se **http://pair-direct.ispto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.



Patent Examiner